REMARKS

STATUS OF THE CLAIMS

Claims 1, 3, 6, 9, 11-15 and 18-25 are pending. Claims 14-15 and 24-25 have been previously withdrawn. By this Amendment, claim 1 has been amended and claim 5 has been cancelled. Support for this amendment can be found in the originally filed specification, for example at pages 5-6. No new matter has been added.

Rejection under 35 U.S.C. §112

Claims 1, 3, 5-6, 9, 11-13 and 18-23 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention for the reasons set forth at pages 2-6 of the Final Office Action. Applicant disagrees for at least the following reasons.

The Examiner has admitted that "the specification defines component to be embedded into the soluble matrix are antigen, MHC molecules, co-stimulatory factors, membrane fragment of antigen presenting cell (APC), bacteria, viruses and combinations thereof"; however, the Examiner has argued that "at the time of filing, applicants are not in possession of any leukocyte stimulation matrix having any 'cell components,' or any 'cell coating' or any combinations thereof, any synthetic antigen obtained from any virus, an [*sic*] bacteria, any fungi, any tumor, any allergens, any endogenous tissue, any fragment of any virus from the family of herpes viruses other than membrane fragments of antigen presenting cell (APC) and viral antigen from cytomegalo virus." *See* pages 3-4 of the Final Office Action. Applicant submits that

claim 5 has been cancelled and presently amended claim 1 does not recite cell components or cell coatings.

However, Applicant disagrees with the Examiner's position that Applicant is not in possession of "any fragment of any virus from the family of herpes viruses other than membrane fragments of antigen presenting cell (APC) and viral antigen from cytomegalo virus." The Examiner is reminded that a claim is not limited to the embodiments described in the specification. MPEP §2111.01(II). "Though understanding the claim language may be aided by explanations contained in the written description, it is important not to import into a claim limitations that are not part of the claim. For example, a particular embodiment appearing in the written description may not be read into a claim when the claim language is broader than the embodiment." *Superguide Corp. v. DirecTV Enterprises, Inc.*, 358 F.3d 870, 875, 69 USPQ2d 1865, 1868 (Fed. Cir. 2004). *See also Liebel-Flarsheim Co. v. Medrad Inc.*, 358 F.3d 898, 906, 69 USPQ2d 1801, 1807 (Fed. Cir. 2004)(discussing recent cases wherein the court expressly rejected the contention that if a patent describes only a single embodiment, the claims of the patent must be construed as being limited to that embodiment).

Applicant submits that membrane fragments of APC and viral antigen from cytomegalo virus are simply non-limiting examples of molecules from the family of herpes viruses that can be used as components for generating a leukocyte stimulation and/or induction of an immunological tolerance. For example, one skilled in the art would know that viral antigens from cytomegalo virus are related to – and would be similar to – viral antigen from other members of the herpes virus family at least because

herpes virus family members share many similar characteristics, including but not limited to virion morphology (*e.g.*, similar capsid structures), core genes, and types of surface glycoproteins and target cells. In other words, one skilled in the art considering the present specification would understand that Applicant was in possession of the present invention, including wherein at least one component for generating a leukocyte stimulation and/or the induction of an immunological tolerance is a virus of the family of herpes viruses or a fragment thereof. Therefore, Applicant respectfully submits that the Examiner's position stated above is untenable.

For at least the foregoing reasons, claims 1, 3, 5-6, 9, 11-13 and 18-23 are in full compliance with 35 USC §112, first paragraph. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection under 35 U.S.C. §103(a)

Andrianov in view of *Vlasselaer*, *Terry*, and *Cima*

Claims 1, 3, 5, 9, 11-13 and 19-23 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent No 5,529,777 to Andrianov et al. (hereinafter "Andrianov") in view of U.S. Patent No 5,663,051 to Vlasselaer (hereinafter "Vlasselaer"), WO 00/27897 to Terry et al. (hereinafter "Terry") and WO 96/27657 to CIMA et al. (hereinafter "Cima") for the reasons set forth at pages 6-9 of the Final Office Action. Applicant disagrees for at least the reasons below.

The Examiner has the initial burden of factually supporting any *prima facie* conclusion of obviousness. If the Examiner does not produce a *prima facie* case, Applicants are under no obligation to submit evidence of nonobviousness. *See* MPEP 2142. The key to supporting any rejection under 35 U.S.C. §103 is the clear articulation

of the reason(s) why the claimed invention would have been obvious. *See Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in KSR International Co. v. Teleflex Inc.*, 72 FR 57526, 57528 (Oct. 10, 2007)(hereinafter "KSR Guidelines"). "Rejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *Id.* (quoting *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, 127 S. Ct. 1727, 82 U.S.P.Q.2d 1385 (2007)). The KSR Guidelines further provide a number of rationales that may be articulated to support a legal conclusion of obviousness. *See* KSR Guidelines at 57529.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the Examiner must explain why the difference(s) between the cited art and the claimed invention would have been obvious to one of ordinary skill in the art. MPEP §2142; *see also* KSR Guidelines at 57528.
Applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness. In particular, the cited references fail to teach or suggest all of the claim elements.

Andrianov teaches that water soluble polymers or polymeric hydrogels are used to encapsulate an antigen to form vaccines. *See* Abstract. The Examiner has argued that *Andrianov* teaches "soluble matrix such as water soluble polymers or polymeric hydrogels for embedding at least any antigen...." *See* page 6 of the Final Office Action.

Yet Applicant notes that *Andrianov* teaches that "the polymers are formed of water soluble polymers...which are crosslinked...to form a water-insoluble hydrogel encapsulating antigen." *See* col. 6, lines 42-45. For example, "the polymers can be crosslinked either by ionic crosslinking or physical crosslinking to render the water-soluble polymers water-insoluble." *See* col. 7, lines 8-10. The present invention, however, teaches that the soluble matrix slowly dissolves within about 4-12 hours in the blood. *See* para. [0030] of the published application. In fact, "the term 'soluble' as used herein means that the soluble matrix dissolves in whole blood within a time range of from hours to a few days." *See* para. [0028] of the published application. (One skilled in the art would understand that whole blood comprises about 55% plasma, which in turn comprises about 90% by volume water. Accordingly, a major portion of whole blood comprises water.) In light of the above, it is clear that *Andrianov* teaches away from the present invention, which teaches a leukocyte stimulation matrix having a soluble matrix, in favor of a water-insoluble microsphere that encapsulates antigens.

Furthermore, as discussed above, *Andrianov* teaches a water-insoluble microsphere that encapsulates antigens. For example, the microspheres containing the antigen can be prepared by mixing the components in an aqueous solution, and then coagulating the polymer together with the substance by mechanical forces to form a microparticle. *See* col. 13, lines 50-54. Accordingly, *Andrianov* fails to teach or suggest a coupling component, as presently claimed, for there is no need – in *Andrianov*, the antigen is trapped within a crosslinked microsphere. *Andrianov* certainly fails to teach or suggest the specific coupling components presently claimed – i.e., cyangoen

bromide, cyanoboro hydride, agarose, agarose derivatives, silane, silane derivatives, and combinations thereof.

Moreover, *Vlasselaer* fails to overcome the deficiencies of *Andrianov*. *Vlasselaer* is directed to an apparatus designed to be used for enriching specific cell types from cell mixtures and a density adjusted cell separation technique used to augment the apparatus. *See* Abstract. The Examiner has argued that *Vlasselaer* teaches "a soluble matrix such as polyethylene glycol (PEG) matrix, long chain sugar such as polysaccharide or agarose, cellulose, or a combination thereof." *See* page 7 of the Final Office Action. Applicant disagrees and submits that *Vlasselaer* teaches density adjusted cell separation (DACS) particles (i.e., silica beads) that were coated with PEG to reduce ionic interactions between proteins and charged surfaces. *See* col. 28, lines 15-19. The DACS particles are added to the cell mixture to be separated in order to bind undesired cells. *See* col. 15, lines 47-49. In other words, the DACS particles are used to bind and remove contaminating cells (e.g., those having densities approximately equal to or lighter than the cells of interest) from the cell mixture during centrifugation. *See* col. 15, lines 25-32 and 48-50. Further, *Vlasselaer* teaches that agarose and cellulose can be DACS particles as discussed above but not that they are a soluble matrix, as the Examiner contends.

The reference also does not teach or suggest "a carrier such as polystyrene latex particle," as the Examiner contends. *See* page 7 of the Final Office Action. Instead, *Vlasselaer* teaches that polystyrene latex particles can be used as DACS particles, which are used to bind and remove contaminating cells. *See* col. 15, lines 48-50 and col. 17, lines 38-40.

Furthermore, *Vlasselaer* does not teach or suggest "a coupling agent such as silane group with alkyl trimethoxy silane to the silica particle," as the Examiner has argued on page 7 of the Final Office Action. The Examiner has cited col. 13, lines 60 bridging col. 14, lines 1-10; however, in the cited passage, *Vlesselaer* teaches that a density gradient material for use in separating cells can be an organosilanized colloidal silica (OCS) particle suspension. At most, the reference teaches that an OCS density gradient material is prepared from colloidal silica by reacting, and thus blocking, the silanol groups with an alkyl trimethoxy silane reagent. However, this is not a teaching or suggestion of a coupling component as presently claimed. It is clear from *Vlasselaer* that the OCS density gradient material does not act as a coupling component – i.e., does not mediate the bonding between the carrier and the one or more component(s) for generating a leukocyte stimulation and/or the induction of an immunological tolerance, as described in para. [0060] of the published application – but is instead used as a density gradient material to separate cells of varying densities. *See* col. 13, lines 13-67.

Additionally, while the Examiner has argued on page 8 of the Final Office Action that "it would have been obvious to one of ordinary skill in the art…to couple any carrier such as polyethylene and polypropylene or polystyrene of *Andrianov*…by substituting the coupling component or cross-linker…of *Andrianov*…with the coupling agent such as silane or silane derivative alkoxy silane as a functional linker as taught by *Vlasselaer*...," Applicant disagrees. As argued above, *Andrianov* fails to teach or suggest a coupling component for there is no need – in *Andrianov*, the antigen is trapped within a crosslinked microsphere. Moreover, one skilled in the art considering *Andrianov* as a

whole would not look to "substitute the cross-linker" in *Andrianov*, as the Examiner suggested, at least because doing so would change the principle of operation of the cited art being modified – i.e., the proposed modification would change the microsphere's crosslinked composition.

The Examiner has made a similar argument with regard to *Terry* – that "it would have been obvious to one of ordinary skill in the art...to couple any carrier such as polyethylene and polypropylene or polystyrene of *Andrianov*...by substituting the coupling component or cross-linker...of *Andrianov*...with the coupling agent such as silane or silane derivative alkoxy silane as a functional linker as taught by *Terry*..." – with which the Applicant also disagrees. One skilled in the art considering *Andrianov* as a whole would not look to *Terry* or *Vlasselaer* – or any other art – to make the Examiner's proposed modification for the reasons discussed above.

Cima also fails to overcome the deficiencies of the cited references discussed above. Applicant disagrees with the Examiner's argument that *Cima* teaches "soluble matrix or carrier such as carboxymethylcellulose and starch" and that it would have been obvious to one of ordinary skill in the art to substitute "the coupling component...of *Cima*...with the coupling agent such as silane or silane derivative alkoxy silane as a functional linker as taught by *Vlasselaer* or *Terry*..." *See* page 8 of the Office Action. Rather, *Cima* teaches that carboxymethylcellulose and starch are examples of water-soluble, biocompatible polymers that can serve as tethers, i.e., molecules that attach growth factors to the solid surface, not a soluble matrix or carrier. *See* page 6, lines 23-28. In fact, *Cima* fails to teach or suggest a soluble matrix at all, much less teach or suggest embedding or covalently linking presently claimed component (c) therein.

Instead, *Cima* discloses that growth effector molecules are tethered (i.e., immobilized) to a substrate such as that described on page 9, lines 9-29.

For at least the foregoing reasons, the Examiner has failed to establish *prima facie* case of obviousness. Reconsideration and withdrawal of the rejection are respectfully requested.

Andrianov, *Vlasselaer*, *Terry*, and *Cima* in view of *Schneck*

Claims 6 and 18 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over *Andrianov* in view of *Vlasselaer*, *Terry*, and *Cima* as applied to claims 1, 3, 5-6, 9, 11-13 and 19-23 and further in view of WO 2004/006951 to Schneck et al. (hereinafter "Schneck") for the reasons set forth at pages 9-10 of the Final Office Action. Applicant disagrees for at least the following reasons.

Claims 6 and 18 depend from independent claim 1 and are patentable for the same reasons. In particular, and as argued above, the combination of *Andrianov*, *Vlasselaer*, *Terry*, and *Cima* fail to teach or suggest presently claimed components a), b), or d). *Schneck* fails to overcome the deficiencies for the same reasons.

For at least the foregoing reasons, the Examiner has failed to establish a *prima facie* case of obviousness. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

Applicant respectfully requests that this Amendment under 37 C.F.R. § 1.116 be entered by the Examiner, placing claims 1, 3, 6, 9, 11-15 and 18-25 in condition for allowance. Applicant submits that the proposed amendment of claim 1 does not raise new issues or necessitate the undertaking of any additional search of the art by the

Examiner, since all of the elements and their relationships claimed were either earlier claimed or inherent in the claims as examined. Therefore, this Amendment should allow for immediate action by the Examiner.

Furthermore, Applicant respectfully points out that the final action by the Examiner presented some new arguments as to the application of the art against Applicant's invention. It is respectfully submitted that the entering of the Amendment would allow the Applicant to reply to the final rejections and place the application in condition for allowance.

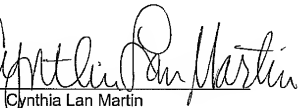
Finally, Applicant submits that the entry of the amendment would place the application in better form for appeal, should the Examiner dispute the patentability of the pending claims.

In view of the foregoing remarks, Applicant submits that this claimed invention, as amended, is neither anticipated nor rendered obvious in view of the prior art references cited against this application. Applicant therefore requests the entry of this Amendment, the Examiner's reconsideration of the application, and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 50-2961.

Respectfully submitted,

Dated: September 28, 2009

By: 

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